UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,342	08/01/2001	Shi-Lung Lin	13761-7024	4134

7590 01/12/2007

WILLIAM E. THOMSON, JR.
HOGAN & HARTSON LLP
BILTMORE TOWER
500 SOUTH GRAND AVENUE, SUITE 1900
LOS ANGELES, CA 90071

EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/920,342	LIN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,34-36,38,40-45,55,58-61 and 63-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,34-36,38,40-45,55,58-61 and 63-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/12/2006 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 09/12/2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 6/12/2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 34-36, 38, 40-45, 55, 58-61 and 63-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting β-cantenin expression *in vivo* in selected organs of chicken embryos using a mRNA-cDNA hybrid duplex, does not reasonably provide enablement for a method of inhibiting expression from any target gene using a mRNA-cDNA hybrid duplex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims

The claims of the instant invention are drawn to a method for inhibiting target gene expression comprising providing a composition comprising or consisting of an mRNA-cDNA hybrid such that the expression of said gene is inhibited and wherein said mRNA is in sense orientation, said cDNA is in the antisense orientation and said mRNA-cDNA hybrid duplex is a complementary region containing more than 500 base pairs. The claims are further limited by requiring that the targeted gene be *in vivo*, or wherein the gene is pathogenic, viral, mutated, or oncogenic in origin, or wherein said cell is eukaryotic, or is from a vertebrate, which may be a mouse. Newly added claims require the mRNA to be a full-length transcript, an unspliced mRNA transcript or a spliced mRNA transcript.

The specification as filed teaches administration of a mRNA-cDNA hybrid duplex targeted to a gene encoding β-cantenin *in vivo* to chicken embryos, wherein the duplex comprises a fragment of the coding region of β-cantenin and further teach inhibition of β-cantenin expression in selected organs of chicken embryos (see Example 8 of the

specification). There is no guidance in the specification as filed that teaches inhibition of expression of any target gene *in vivo* after administration of a mRNA-cDNA hybrid duplex.

The following factors have been considered in the analysis of enablement: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claimed breadth of claims 32, 34-36, 38, 40-45, 55, 58-61 and 63-71 encompass methods of inhibiting any target gene expression comprising providing a composition comprising or consisting of an mRNA-cDNA hybrid such that the expression of any target gene is inhibited. Although the specification teaches inhibition of β-cantenin expression in selected organs of chicken embryos after administration of a mRNA-cDNA hybrid duplex, this guidance is not sufficient to resolve the known unpredictability in the art associated with inhibition of gene expression using RNA-DNA hybrid duplexes.

While the level of one of ordinary skill practicing the invention would be high, the level of predictability is considered to be variable as evidenced by the references cited herein. Parrish et al. teach administration of a RNA-DNA hybrid duplex targeted to a *unc-22* gene of *C. elegans* wherein said RNA-DNA hybrid duplex did not silence gene expression (see Figure 5 page 1081). Parrish et al. teach the loss of *unc-22* expression

of *C. elegans* is responsible for a twitching phenotype and *C. elegans* administered a RNA-DNA duplex did not produce the characteristic twitching phenotype associated with loss of *unc-22* expression. Likewise, Tuschl et al. (WO 02/44321) has demonstrated the unpredictability of inhibition of gene expression using a RNA-DNA hybrid duplex (see Figure 14). Tuschl et al. teach luciferase gene expression was not inhibited in cells after treatment with a RNA-DNA hybrid duplex.

Thus, the instantly claimed invention is not described in the prior art or the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. One of skill in the art could not practice the methods of inhibiting expression from any target gene using a RNA-DNA hybrid duplex without undue, *de novo* trial and error experimentation, because as demonstrated above, it is well known that there is a high level of unpredictability in the art for gene silencing of target genes using a RNA-DNA hybrid duplex. Further, given the teachings of the specification as discussed above, one skilled in the art would not know *a priori* whether introduction of any RNA-DNA duplex by the broadly disclosed methodologies of the instantly claimed invention, would result in successful inhibition of expression of any target gene.

To practice the claimed invention, a number of variables would have to be optimized including 1) determining a specific target sequence, 2) targeting the RNA-DNA hybrid to said particular sequence, 3) determining the binding of said RNA-DNA hybrid duplex to said particular nuclei acid sequence such that sufficient inhibition of gene expression occurs. While determination of a particular sequence to target gene

and targeting a particular hybrid duplex to said gene may be routine, when taken together to target any gene in any cell such than inhibition of gene expression occurs, the amount of experimentation required becomes such that one of skill in the art could not practice the claimed invention with a substantial amount of trail and error experimentation.

Response to Arguments

Re: Claim Rejections - 35 USC § 102 and 103

The rejection of record of claims 32, 34, 35, 41-43, 55, 58, 59, and 64-66 under 35 U.S.C. 102(a) as being anticipated by Alexeev et al. (Nature Biotech. 2000, 18:43-47) is withdrawn in response to claim amendments filed 09/12/2006.

The rejection of record of claims 32, 34-38, 40-45, 55, 58-61 and 63-68 under 35 U.S.C. 103(a) as being unpatentable over Alexeev et al. (cited above) as applied to claims 32, 34, 35, 41-43, 55, 58, 59, and 64-66 above, and further in view of Fire et al. (U. S. Patent Number 6,506,559), and Bennett et al. (U. S. Patent Number 6,066,500), is withdrawn in response to claim amendments filed 09/12/2006.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635

SEAN MCGARRY
PRIMARY EXAMINER
AU 1635